TRIAZOLE AS ANTI-INFLAMMATORY AGENT: A SHORT REVIEW

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Abstract: Triazole is a five-member heterocyclic ring compound, containing two carbon and three nitrogen atoms with molecular formula $C_2H_3N_3$. Triazole exists in two isomeric forms 1, 2, 3-triazole and 1, 2, 4-triazole. The triazole nucleus is a normal and integral characteristic of a number of natural products and pharmaceutical agents, and it is one of the most significant and well-known heterocycles. Triazole and its derivatives show great importance in biological activities such as, anti-inflammatory, analgesic, antiepileptic, antineoplastic, antihypertensive, antimalarial, local anaesthetic, antianxiety, antidepressant, antihistaminic, antioxidant, anticonvulsant and antiviral. The present review provides a broad view of the anti-inflammatory activity possessed by compounds having a triazole nucleus.

Keywords **- Triazole, Biological activity, Anti-inflammatory, antiviral.**

INTRODUCTION

Tiazoles are the class of heterocyclic compounds which are under study for many years. Triazole is an organic compound that has two isomers. Its molecular formula is C2H3N3. The azole ring in triazoles can bind to a wide range of enzymes and receptors in biological systems. As a result, it demonstrates a wide range of biological processes. [1-3]

Heterocyclic chemistry has evolved into a distinct branch of chemistry with a long tradition, current culture, and promising future prospects. The most well-known hetero atoms are nitrogen, oxygen, and sulfur. [4] One of the most difficult things for a medicinal chemist is to find new agents. Because of their utility in a variety of applications, the synthesis of high nitrogen containing heterocyclic systems has gotten a lot of attention in the last decade. The triazole is a compound identified by the inclusion of three nitrogen heteroatoms in a five-membered ring structure. The 1, 2, 3-triazole and the 1, 2, 4-triazole are the two tautomeric forms. The nucleus 1H and 4H- 1, 2, 4-triazole are regarded as pharmacologically significant nuclei. [5, 6]

Due to their proven effectiveness in suppressing pain and inflammation, nonsteroidal anti-inflammatory drugs (NSAIDs) are the most commonly used anti-inflammatory drugs in the world. Medicinal studies have recently focused their attention on finding safer and more reliable NSAIDs. Triazole derivatives, especially triazole-modified NSAIDs, showed greater promise as anti-inflammatory drugs. [7] Another heterocyclic ring with medicinal potential in humans is the 1, 2, 4-triazoles. Biological activity findings on the 1,2,4-triazole ring system suggest that it is a fascinating class of heterocyclic compounds with a wide range of pharmacological effects, including antifungal [8], anti-inflammatory, analgesic [9], anthelmintic [10], antibacterial [11] ,antitumor [12], antihypertensive, antidepressant, anticonvulsant and antiviral.[13] Inflammation is a multifaceted phenomenon. It represents organisms' responses to various stimuli and is linked to a variety of disorders, including arthritis, asthma, and psoriasis, that necessitate long-term or repeated care. Two isoforms of cyclooxygenase are COX-I and COX-II. COXs are essential enzymes in the biosynthesis of prostaglandins (PGs) from arachidonic acid (AA) and play a role in inflammation. In the gastrointestinal (GI) tract, constitutive COX-1 provides cytoprotection, while inducible COX-2 mediates inflammation. [14, 15]

Nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly used to treat inflammation-related symptoms, especially arthritic pain. Aspirin, diclofenac, flurbiprofen, and ibuprofen are examples of traditional non-steroidal anti-inflammatory medications (NSAIDs) that work by inhibiting the COX-1 isoenzyme or by inhibiting both COX-1 and COX-2 isoenzymes. They are, however, more selective for COX-1 than COX-2. [16, 17] The triazole ring system is of particular interest, especially within medicinal chemistry because of its versatile biological activity and clinical applications. [18, 19]

Ibuprofen, a well-known nonsteroidal anti-inflammatory drug (NSAID), is commonly used in the treatment of pain and inflammation due to its high curative effectiveness and low risk of side effects. Its structurally adapted derivatives, which substitute the carboxyl group with a triazole ring, have stronger anti-inflammatory properties than ibuprofen, and some of them

are also more potent than diclofenac. Triazole Schiff base has far stronger anti-inflammatory properties than ibuprofen and diclofenac and analgesic effects comparable to diclofenac.[20] Intensive study has been focusing on the anti-inflammatory function of the triazole nucleus as a consequence of the extraordinary pharmacological performance of triazole derivatives. The present review highlights the anti-inflammatory activity of triazole and its derivatives.

Chetan M. Bhalgat et al [21] synthesized some new dihydropyrimidinecarbonitrile and its triazole fused derivatives. The derivatives were characterized by spectral data and elemental analysis and these compounds were used for their antioxidant and anti-inflammatory screening. Compound (**Figure 1**) is one of the final triazole derivatives of pyrimidine which show antioxidant and anti-inflammatory activity. Synthesized compounds were also tested for anti-inflammatory activity, compared to the standard diclofenac sodium; they have shown acceptable anti-inflammatory activity.

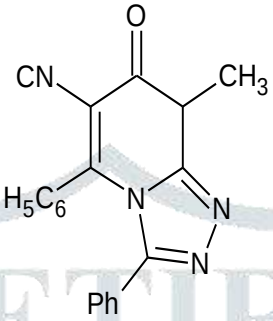


Figure 1.

Rajasekaran, et al[22] synthesized and tested a series of novel 1-(2-(1-Tosyl- -1*H*-tetrazol-5-yl)ethyl)-1*H*-benzo[*d*][1,2,3]triazole (**Figure 2a**) and 4,5-(2-(1*H*-benzo[*d*][1,2,3]triazo-1-yl)ethyl)-1*H*-tetrazol-1-yl sulfonyl)benzenamine **(Figure 2b**) elicited superior anti-inflammatory activity. The anti-inflammatory activity was examined by the carragenean induced paw edema method.

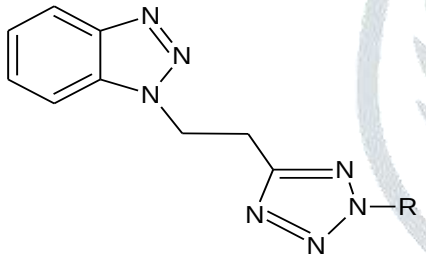


Figure 2.

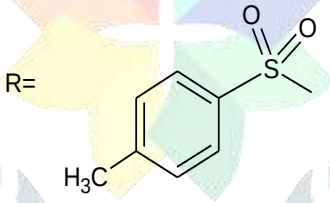


Figure 2a.

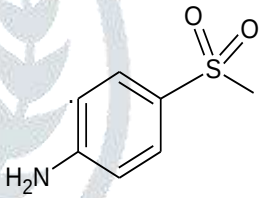
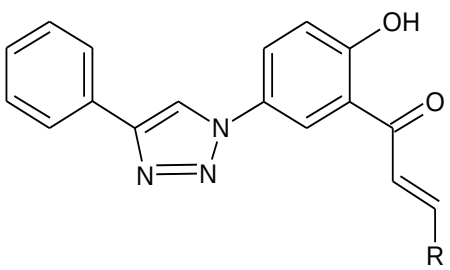


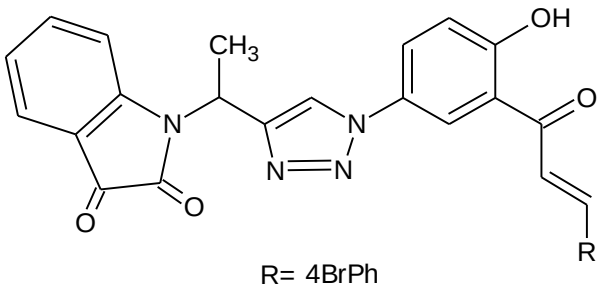
Figure 2b.

Boshra et al [23] studied some novel series by hybrid pharmacophore approach is used to design and synthesize 2'-hydroxychalcone-triazole hybrid molecules. Carrageenan mediated paw edema bioassay in rats with celecoxib as a reference drug was used to screen the most potent compounds in vitro for in vivo anti-inflammatory studies. The percent of edema inhibition was measured after the test compound was given i.p. at a dosage of 28 M/kg. The findings indicated that the anti-inflammatory activity of the majority of the studied compounds increased gradually over time, peaking after 3 hours, while compounds (**Figure 3**) and (**Figure 4**) maintained their activity for up to 5 hours.



R= 4BrPh

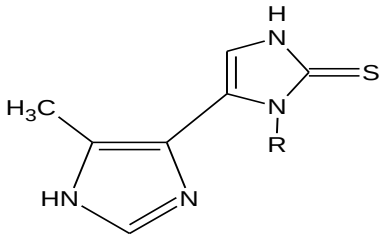
Figure 3.



R= 4BrPh

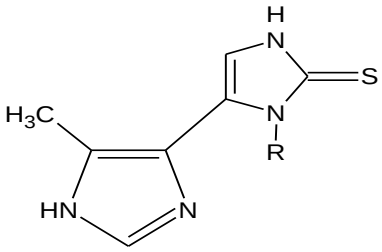
Figure 4.

Almasirad et al [24] designed and synthesized new imidazolyl-1, 3, 4-oxadiazoles and 1, 2, 4-triazoles by molecular hybridization. The synthesized compounds were tested by writhing and carrageenan mediated rat paw edema experiments. Compounds (**Figure 5**), (**Figure 6**) were active anti-inflammatory agents (33-43% inhibition) after 5 h in comparison with control and their activity was comparable to indomethacin.



R=Methyl

Figure 5.



R=4 Methylphenyl

Figure 6.

Birsen et al [25] mentioned and prepared novel compound 3-[1-(4-(2 methylpropyl) phenyl) ethyl]-1,2,4-triazole-5-thione and its derivatives 6-benzylidenethiazolo[3,2-b]-1,2,4-triazole-5(6H)-ones. Spectral and elemental analysis is used to deduce the structures of the compounds (**Figure 7**). Anti-inflammatory properties of these compounds have been screened in pharmacological trials. The synthesized compounds were normally considered to be safe at a dosage level of 200 mg/kg in gastric ulceration trials.

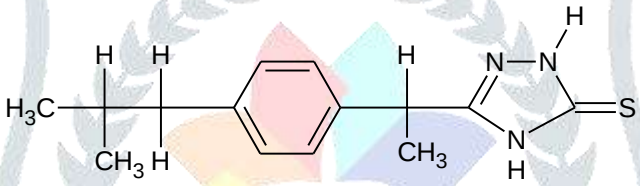


Figure 7.

Ashraf et al [26] reported the compounds 1, 2, 4-triazole-3-acetates (**Figure 8**). The anti-inflammatory properties of the synthesized compounds were investigated. The majority of the compounds studied had strong anti-inflammatory effects, according to the findings. Anti-inflammatory properties, as well as gastric ulcerogenic effects and acute toxicity, were assessed in the compounds collected.

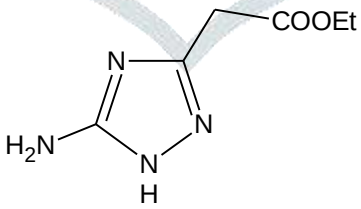


Figure 8.

Assarzadeh et al [27] prepared new thiazolo[3,2-b][1,2,4]triazole-6(5H)-ones with 2-phenoxyphenyl and various aryliden and heteroaryliden moieties were synthesized and their anti-inflammatory and analgesic activities were screened in vivo by writhing and carrageenan-induced rat paw edema tests. The majority of them were found to be more active analgesics than mefenamic acid, and the majority of the final products had strong anti-inflammatory activity.

Kumudha et al [28] synthesized a new series of substituted 1,2,4-triazoles as substituted 4,5-diphenyl *4H*-1,2,4-triazole-3-thiols and evaluated for their anti-inflammatory, anticonvulsant antibacterial, antifungal activities. Almost all of the compounds had anti-inflammatory, anticonvulsant, and antimicrobial properties that ranged from strong to mild.

Abdel-Megeed et al [29] synthesized different acylated 1, 2, 4- triazole-3-acetates. The anti-inflammatory properties of the synthesized compounds were investigated .In the carageenan-induced rat paw edema survey, the most studied compounds displayed strong anti-inflammatory behavior with low gastric ulcerogenicity as compared to indomethacin.

CONCLUSION

Triazole has a unique moiety that is responsible for various biological activities. Triazole and its derivatives have a variety of pharmacological activities, their function as an anti-inflammatory agent has been well established. There is also space for further study in this area in order to discover a novel anti-inflammatory agent. This analysis would be beneficial to researchers in this area.

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CONFLICT OF INTEREST

The author declares that he do not have any conflict of interest.

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